

US005824659A

United States Patent [19]

Strickland et al.

[11] **Patent Number:** 5,824,659

[45] **Date of Patent:** Oct. 20, 1998

[54] CYTOPROTECTIVE OLIGOSACCHARIDE FROM ALOE PREVENTING DAMAGE TO THE SKIN IMMUNE SYSTEM BY UV RADIATION

[75] Inventors: Faith M. Strickland; Ronald P. Pelley, both of Galveston; Margaret L.

Kripke, Kingwood, all of Tex.

[73] Assignee: Board of Regents, The University of

Texas System, Austin, Tex.

[21] Appl. No.: 697,974

[22] Filed: Sep. 4, 1996

[51] **Int. Cl.**⁶ **A61K 31/715**; C08B 37/00; C07G 3/00

[52] **U.S. Cl.** **514/54**; 514/885; 536/123; 536/123.1; 536/124; 536/127; 536/128

[56] References Cited

U.S. PATENT DOCUMENTS

| 3,103,466 | 9/1963 | Farkas | 167/58 |
|-----------|---------|-----------------|-----------|
| 3,878,197 | 4/1975 | Maret | 260/236.5 |
| 3,892,853 | 7/1975 | Cobble | |
| 4,178,372 | 12/1979 | Coats | 424/195 |
| 4,500,510 | 2/1985 | Goldstein | 424/80 |
| 4,585,656 | 4/1986 | Rosenthal et al | 424/195.1 |
| 4,593,046 | 6/1986 | Gruber | 514/717 |
| 4,627,934 | 12/1986 | Lindauer et al | 252/552 R |
| 4,670,265 | 6/1987 | Sydiskis et al | 424/195.1 |
| 4,735,935 | 4/1988 | McAnalley | 514/53 |
| 4,788,007 | 11/1988 | Baron | 252/589 |
| 4,851,224 | 7/1989 | McAnalley | 424/195.1 |
| 4,959,214 | 9/1990 | McAnalley | 424/195.1 |
| 4,966,892 | 10/1990 | McAnalley | 514/54 |
| 5,356,811 | 10/1994 | Coats | 435/267 |
| 5,441,943 | 8/1995 | McAnalley et al | 514/54 |
| | | | |

OTHER PUBLICATIONS

Wang et al., Zhiwu Xuebao, 31(5): 389–392, (1989) ** Abstract Only.

Pelley et al., Seifen, Oele Fette, Wachse, 119 (5): 255–268, (1993).

International Search Report dated Jan. 14, 1998 (PCT/US97/17322) (UTFG: 207P).

Strickland et al., "Prevention of ultrviolet radiation—induced suppression of contact and delayed hypersensitivity by *Aloe barbadensis* gel extract," *J. Invest. Dermatol.*, 102(2):197–204, 1994.

Vilkas and Radjabi–Nassab, "The glucomannan system from *Aloe vahombe (liliaceae)*, III. Comparative studies on the glucomannan components isolated from the leaves," *Biochimie*, 68:1123–1127, 1986.

Wang and Waller, "Current status of quality control of *Aloe barbadensis* extracts," *SÖFW–Journal*, 119:255–268, 1993.

Andersen et al., "Ultraviolet B Dose-Dependent Inflammation in Humans: A Reflectance Spectroscopic and Laser Doppler Flowmetric Study Using Topical Pharmacologic Antagonists on Irradiated Skin," *Photodermatol., Photoimmunol. & Photomed.*, 9:27–23, 1992.

Bergstresser, "Sensitization and Elicitation of Inflammation in Contact Dermatitis," *Immunology Series*, 46:219–245, 1989

Davis et al., "Processed Aloe vera Administered Topically Inhibits Inflammation," J of the American Podiatric Medical Association, 79(8):395–397, Aug. 1989.

Gowda, Structural Studies of Polysaccharies from *Aloe* saponaria and *Aloe* vanbalenii, Carbohydrate Research, 83:402–405, 1980.

Gowda et al., Structural Studies of Polysaccharides from *Aloe vera, Carbohydrate Research*, 72:201–205, 1979.

Kripke, "Effects of UV Radiation on Tumor Immunity," *Journal of the National Cancer Institute*, 82(17):1392–1396, Sep. 1990.

Lee, "Our Thanks to Roche Dermatologics, Division of Hoffmann-La Roche Inc." *The Journal of Investigative Dermatology*, 606–610, 1991.

Mandal et al., "Characterization of Polysaccharides of *Aloe Barbadensis* Miller: Part III—Structure of an Acidic Oligosaccharide," *Indian Journal of Chemistry*, 22B:890–893, Sep. 1983.

Mandal and Das, "Structure of the D-Galactan Isolated from Aloe Barbadenis Miller," Carbohydrate Research, 86:247–257, 1980.

Mandal and Das, "Structure of the Glucomannan Isolated from the Leaves of *Aloe barbadensis* Miller," *Carbohydrate Research*, 87:249–256, 1980.

Paulsen et al., "Structural Studies of the Polysaccharide from *Aloe Plicatilis* Miller," *Carbohydrate Research*, 60:345–351, 1978.

Pelley, "Aloe Polysaccharides and Their Measurement," *Inside Aloe*, Supplement, pp. 1–4, Feb. 1996.

Radjabi et al., "Structural Studies of the Glucomannan from *Aloe vahombe,*" *Carbohydrate Research*, 116:166–170, 1983.

Radjabi–Nassab et al., "Further Studies of the Glucomannan from *Aloe vahombe* (liliaceae). II. Partial Hydrolyses and NMR ¹³C Studies," *Chimie*, 66:563–567, 1984.

(List continued on next page.)

Primary Examiner—John Kight Assistant Examiner—Howard C. Lee Attorney, Agent, or Firm—Arnold, White & Durkee

[57] ABSTRACT

The present invention relates to a glucose-rich, mannosecontaining oligosaccharide described herein has a molecular weight of approximately 1,000-5,000 daltons and is separated from interfering aloe components. The oligosaccharide inhibits loss of skin immunocompetency which is induced by ultraviolet irradiation. The oligosaccharide is obtained by cellulase cleavage of a precursor block polysaccharide of Aloe (FIG. 1) and has about 75% glucose, about 25% mannose and trace galactose. The precursor polysaccharide has a molecular weight of >2,000,000 daltons, is about 73% hexose with a total hexose to reducing sugar ratio of about 23:1. This polysaccharide is about 7% glucose, about 85% mannose and about 4% galactose. Also described is a method for obtaining an immunoprotective oligosaccharide by treating an Aloe extract with cellulase at a concentration of less than about 2 grams per 215 liters.

6 Claims, 12 Drawing Sheets